

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

**Miri Seiberg, et al.**

Serial No. **09/206,249**

Art Unit: **1651**

Examiner: **M. Meller**

Attorney Docket No.: **JBP 438**

**METHOD FOR REGULATING  
PHAGOCYTOSIS**

**DECLARATION OF ROBERT ZIVIN, PH.D.**

I, Robert Zivin, am a Corporate Director in the Corporate Office of Science and Technology at Johnson & Johnson. My education includes a Ph.D. in Microbiology from University of Chicago and a B. S. in Biology from the Northern Illinois University. My curriculum vitae is attached hereto as Exhibit 1.

1. This Declaration is respectfully submitted to discuss the process of denaturation of proteins. Proteins are defined by both (1) their chemical structure, which includes its substituent amino acids as well as their unique conformation and (2) their biological function. Only when a protein has its unique chemical structure and conformation does it exhibit its biological function or activity.

2. Proteins are made by joining amino acids by a peptide bond, which is formed in a reaction between the amino group of one amino acid and the carboxyl group of another amino acid. (Messier, P., "Protein Chemistry of Albumen Photographs", *Topics in Photographic Preservation*, Vol. 4, 1991, pp. 124-135, <http://albumen.stanford.edu>).

3. Proteins have a particular conformation that is characteristic of each specific type. This conformation forms as a result of the interactions of the protein's

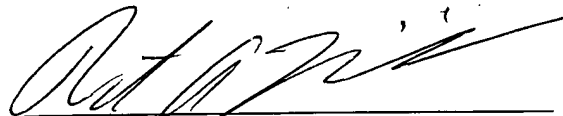
component amino acids as they seek the lowest free energy state for the protein. (Messier, P., 1991). "Only when in its native, or low energy, state does a protein manifest all of its characteristic properties and biological functions..." (Messier, P., 1991). Thus, conformation is an important aspect of protein structure and identification.

4. "Protein denaturation" is defined as "the process of altering the native/low free energy conformation of a protein." (Messier, P., 1991). Once the protein is denatured, by exposure to increased temperature, its characteristic activity is no longer present and it cannot be detected in a composition. Denaturation generally only alters the conformation of a protein and does not chemically break the peptide bonds. In theory, this process may be reversible with some proteins.

5. However, in the case of most proteins, including those proteins contained in soy exhibiting Soy Trypsin Inhibition ("STI") activity, denaturation is irreversible. Soy proteins are soluble proteins—they are folded such that their hydrophobic substituents are internal to the conformation. Denaturation opens up the conformation, exposing the inner hydrophobic substituents. This often causes the denatured proteins to precipitate out of solution, removing them from the composition in which they reside. However, in any case, the elimination of biological activity is independent of the presence or absence of the denatured protein.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of title

18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

A handwritten signature in black ink, appearing to read "Robert Zivin", written over a horizontal line.

Dr. Robert Zivin

12/23/03

Date